conduction abnormalities and increasing myelination on MRI scans. Pts transplanted later in the course of the disease have had less dramatic but measurable improvements, particularly in language and cognitive skills. We hypothesized that UCB-derived cells migrated to brain and differentiated into non-hematopoietic cells in these pts but could not study this further with non-invasive techniques. Unfortunately, one baby with advanced Krabbe disease, transplanted with a UCB donor of the opposite sex at 8 months of age, died 1 yr post transplant. Her brain was studied to determine whether donor derived cells were present at the time of her death. Brain tissue was fixed in formalin, sectioned and stained with histochemical stains for glial and neuronal tissues and counterstained with FISH for the XY chromosomes to differentiate donor and host cells. We found extensive distribution of host cells in blood vessels, peri-ventricular tissues, white matter of the cerebral cortex, cerebellum, choroid plexis and forebrain parenchyma. Differentiation of donor cells to microglia and choriod plexus cells was present, but differentiation into cells of neuroectodermal origin (e.g neurons, astrocytes, or oligodendrocytes) was not found. These results demonstrate that donor-derived UCB cells can extensively distribute in brain tissues after UCB transplantation. Transdifferentiation across germ cell layers was not demonstrated.

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EMBRYONIC STEM CELLS SURVIVE AND PROLIFERATE AFTER INTRA-PERITONEAL IN UTERO TRANSPLANTATION AND PRODUCE TERATOCARCINOMAS

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Embryonic stem cells (ESC) support murine fetal development if injected in blastocysts and can engraft in conditioned newborns. However, little is known about their behavior after the in utero transplantation. The aim of this research is to establish a model for study of the in vivo differentiation of ESCs after the in utero transplantation. We hypothesize that the in utero transplanted ESC integrate into the fetus and, based on their pluripotency, may represent a therapeutic alternative for prenatally diagnosed diseases. ESC genetically engineered to express yellow fluorescent protein (YFP-ESC) were transplanted intra-peritoneally in utero at E14-15. The presence of YFP signal was analyzed in various tissue of the viable offsprings at different ages (4-8 weeks) and was quantified by digitalized fluorescence microscopy on analysis of tissue supernatants. The YFP-ES-derived cells were found only in the liver without any evidence of YFP signal in other organs. Extensive peritoneal teratocarcinomas with supradiaphragmatic involvement was generated after the ESC in in utero transplantation in allogeneic mice. Also, clinical and histopathological pictures suggestive of graft-versus -host disease were present in two out of five haploidentical mice. Studies that address the issue of ESC differentiation into hepatic cells within this model are in process and will be presented. The promise and the potential risks of the ESC transplantation have to be carefully considered.

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BRAIN FROM BLOOD IN HUMANS

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Adult hematopoietic stem cells (HSC) have the capacity to self-renew and differentiate into all hematopoietic lineages. Recent studies in humans have found that bone marrow derived stem cells can function as regenerative progenitors for the liver, kidney, heart, musculoskeletal tissue, and gastrointestinal tract. In the brain, animal studies have found that murine HSC can differentiate into neurons of the adult mouse. Following these reports, we investigated whether human HSC contribute to adult human neurogenesis. Autopsy brain specimens from female recipients of therapeutic HSC transplantation from male donors where analyzed for cells containing Y chromosome. In these cases, hippocampal cells containing Y chromosome were found. Most Y-positive cells were non-neuronal, with transgender neurons (beta-3-tubulin positive) comprising only 1% of total neurons. In addition, these Y-chromosome neurons were not a product of fusion, as evidenced by presence of only one X chromosome. Our findings demonstrate that postnatal human neuropoiesis is present and that human hematopoietic cells have the capability to generate neurons, albeit at a very low level. The biologic implications suggest that the HSC or a hematopoietic progenitor responds to instructive neurotrophic cues, crosses the blood-brain-barrier, diffuses into central nervous system tissues and activates previously dormant neuron-specific genetic programming. Together these observations challenge the restricted notion of unidirectional ontogenic maturation and uncover a mounting HSC plasticity repertoire. Our findings also suggest that human HSC may serve as a therapeutic source for regenerative neuropoiesis.

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AUTOLOGOUS STEM CELL COLLECTION IN POLYCYTHEMIA VERA

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Allogeneic Tx can eradicate MF. We reported resolution of MF after ablative syngeneic Tx in a patient with spent phase PV (B J Haematol 117:246). Hence GvL is not required to eliminate MF. Ablation with ASCT could represent a major advance for spent phase PV. In PV, the optimal timing and the influence of organomegely, myelosuppression and MF on autologous collection are uknown. Between 08/94 and 01/02, 16 pts with PV underwent stem cell collection. Mobilization was G-CSF 10 mcg/kg x 5d. Minimum target was 2.5 X 10^6 CD34+/kg. All myelosuppression but anagrelide was stopped a minimum of 2 wks before collection. M:F ratio was 7/9. Median ages at Dx and collection were 47 and 57. Organomegaly was present in 10 pts (63%) and moderate or extensive MF in 4 pts (25%). Seven pts were receiving myelosuppression. Three pts had clonal cytogenetic abnormalities. For the whole cohort median TNC and CD34+ counts were 8.3 X 10^8/kg and 4.98 X 10^8/kg. No organomegaly predicted for higher TNC and lower CD34+ contents but differences were NS (p=0.16 and 0.1). MF adversely affected TNC (p=0.05) but not CD34+ (p=0.8). Time from Dx and myelosuppresion had no influence on TNC and CD34+ . One pt had CD34+ below target (2.2 X 10^6/kg). See table for details. Autologous collection of peripheral blood stem cells is feasible in PV pts several years after DX. Organomegaly and MF are not contraindications for collection. Myelosuppresion up to 2 weeks prior to mobilization appears safe in terms of cell contents. Studies are now required to determine the safety and efficacy of ablation and ASCT to reestablish effective hematoposiesis in spent PV.

	TNC e8/kg		CD34+ e6/kg	
	N	Y	N	Y
Organomegaly	12.2	6.6	3.06	8.30
T from Dx>10y	0.7	8.7	2.9	11.9
MF	10.3	3.8	6.09	3.25
Myelosuppression	8.4	9.1	3.7	9.8

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PREFERENTIAL EXPANSION OF CORD BLOOD EARLY PROGENITORS ENABLED BY LINEAR POLYAMINE COPPER CHELATORS

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We demonstrated that the polyamine copper chelator, tetraethylenepentamine (TEPA), extended the long term cord blood CD34+ cultures (Peled et al, Brit. J. Haematol. 116:655 2002).To study the effect of TEPA on long-term expansion, we adopted a